

### **REMARKS**

With entry of the present amendment claims 4, 11, 12, and 28 to 30 are pending. Claims 28 and 29 have been amended to correct the dependency. The amended claims are supported by the specification and claims as filed. No new matter has been added by this amendment.

This response is accompanied by a Request for a three-month extension of time and authorization to charge Deposit Account No. 08-2525 in the amount of 1,020.00 for the extension fee. No additional fees are believed due. However, the Director is hereby authorized to charge any deficit, or credit any overpayment, to Deposit Account No. 08-2525.

### **REJECTION OF CLAIMS 28 AND 29 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

Claims 28 and 29 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite for being dependent upon a cancelled base claim. Claims 28 and 29 have been amended to depend from claim 4, rendering the rejection moot.

### **REJECTION OF CLAIMS UNDER THE JUDICIALLY CREATED DOCTRINE OF OBVIOUSNESS-TYPE DOUBLE PATENTING**

Claims 4 and 11 to 12 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 to 4 of commonly owned U.S. Patent 6,849,624 (issued from application no. 10/196,795). In making this rejection, the Office Action states that while the claims are not identical, they are not patentably distinct because the instant claims are simply a different crystalline form of one of the compounds encompassed by the claims of the '624 patent and that the properties recited in claim 4 are presumed to be inherent in the compound of the '624 patent. The rejection further states that the composition of claims 11 and 12 would be obvious over the claims of the '624 patent because when dissolved in water, the two different forms of 2-(3,5-bis-

trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 $\lambda^6$ -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide would be the same.

Applicants respectfully traverse this rejection in part because the specific crystalline polymorph claimed in the instant application is physically distinct from the polymorph described in the '624 patent, resulting in improved pharmacologic properties and because the claimed composition requires that the compound be present in crystalline form A.

As disclosed in the instant application, the compound 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 $\lambda^6$ -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide exists in four distinct forms: crystalline forms A, B, and C and an amorphous form. (¶ [0005]) That the compound exists in these four distinct forms was not known at the time of the '624 invention.

As also disclosed in the instant application, each of the four forms of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 $\lambda^6$ -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide are prepared by different methods (¶¶ [0030] to [0037]) and have different physiochemical properties, such as different X-ray diffraction patterns, different IR spectra, different DSC, and different DVS (¶¶ [0038] to [0042]). Due to these different properties, the claimed form A provides improved bioavailability, especially for oral delivery, than the other forms. While the amorphous form also exhibits improved bioavailability over the B and C forms, it is not suitable for oral delivery. (¶¶ [0020] and [0021]).

Enclosed herewith is the declaration of Dr. Olaf Grassmann. As noted in the declaration, the 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 $\lambda^6$ -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide compound described in the '624 patent is form B. (¶¶ 7 to 9, Exhibit 2) The declaration also shows that form A has a different X-ray

diffraction pattern, a different IR spectrum, and a different DSC from form B. (¶¶ 10 to 13, Exhibits 2 & 3, and Figures 1, 2 & 4 of the instant specification.)

Contrary to the Patent Office position that the properties of the claimed compound are inherent in the compound of the '624 patent, it is evident from the data in the specification and the declaration of Dr. Grassmann that the compound of the instant claims, form A, is different from and has improved pharmacological properties over form B of the '624 patent. Thus, the instant claimed compound is not obvious in view of the compound recited in the claims of the '624 patent.

With respect to claims 11 and 12, the Office Action states that even if the crystalline form of the instant claims is different from the crystalline form of the '624 patent, the pharmaceutical compositions of these two crystalline forms are presumed to be the same, because when dissolved in water, the compounds will no longer be in crystalline form and will be identical. However, this rationale fails to consider all of the limitations of instant claims 11 and 12. Claim 11 requires that the compound be present in the composition in crystalline form A. Thus, to the extent that dissolving the compound in water would result in something other than form A, i.e. form B or amorphous, it is not encompassed by the claim. Further, claim 12 depends from claim 11 and specifically recites that the compound of form A be present as a powder in a gelatine capsule, which excludes a water solution. Thus, claims 11 and 12 require that the compound 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 $\lambda$ <sup>6</sup>-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide exist in crystalline form A, which is distinct and non-obvious in view of crystalline form B of the '624 patent as discussed above.

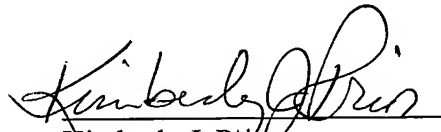
For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejection and allowance of claims 4, 11, 12, and 28 to 30.

Serial No. 10/766,122  
Filed: January 27, 2004

The foregoing amendment is fully responsive to the Office Action issued January 12, 2006. Applicants submit that Claims 4, 11, 12, and 28 to 30 are allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Kimberly J. Prida", written over a horizontal line.

Kimberly J. Prida  
Attorney for Applicant(s)  
(Reg. No. 41,483)  
340 Kingsland Street  
Nutley, New Jersey 07110  
Telephone: (973) 235-6208  
Telefax: (973) 235-2363

245821